Claims

1. A composition consisting of :

a first sustained release formulation of a gonadotropin hormone releasing hormone composition capable of releasing the gonadotropin hormone releasing hormone composition during a period of at least about one month at a rate sufficient to induce and maintain chemical castration of a male patient, and

a second sustained release formulation of an estrogenic composition capable of maintaining for said period a serum level sufficient to reduce the enhanced loss of bone mineral density or the hot flashes that are normally caused by the administration of a gonadotropin hormone releasing hormone composition that chemically castrates a male patient,

characterised in that said second sustained release formulation releases an estrogenic composition under a profile comprising at least a first initial phase and a second phase, the release of the estrogenic composition in the course of said second phase being at a rate between about 10 and 100 µg of estradiol equivalent per day, the release of the estrogenic composition in the course of said first initial phase never exceeding 5 times the daily release of the estrogenic composition occurring during said second phase.

2. The composition according to claim 1, characterised in that said first sustained release formulation of a gonadotropin hormone releasing hormone composition is capable of releasing the gonadotropin hormone releasing hormone composition at a rate between about 10 and about 1,000 µg per day.

3. A composition consisting:

a first sustained release formulation of a gonadotropin hormone releasing hormone composition capable of releasing the gonadotropin hormone releasing hormone composition for a period of at least about one month at an average rate between about 10 and 1,000 µg per day, and

a second sustained release formulation of an estrogenic composition capable of releasing the estrogenic composition under a profile comprising at least a first initial phase and a second phase, the release of the estrogenic composition in the course of said second phase being at a rate between about 10 and 100 μg of estradiol equivalent per day, the release of the estrogenic composition in the course of said first initial phase never exceeding 5 times the upper daily release of the estrogenic composition occurring during said second phase.

4. The composition according to any of the preceding claims, characterised in that the gonadotropin hormone releasing hormone composition is selected from the group consisting of gonadotropin hormone releasing hormone, agonists of gonadotropin hormone releasing hormone, antagonists of gonadotropin hormone releasing hormone and mixtures thereof.

5. The composition according to claims 1, 2, or 3, characterised in that the gonadotropin hormone releasing hormone composition is a gonadotropin hormone releasing hormone agonist selected from the group consisting of leuprorelin, goserelin, triptorelin, buserelin, nafarelin, deslorelin, histerelin, gonadorelin, and salts and mixtures thereof.

6. The composition according to claims 1, 2, or 3, characterised in that the estrogenic composition is selected from the group consisting of chlorotrianisene, dienestrol, diethylstilbestrol, diethylstilbestrol dipropionate, diethylstilbestrol monobenzyl ether, equilelinin, equilelinin sulfate, estetrol, estradiol, (3α,17β)-estr-4-ene-3,17-diol, estriol, estriol hemisuccinate, estrone, estrone sulfate monosodique, estrone potassium sulfate, ethinylestradiol, fosfestrol tetrasodique, hexestrol, hydroxyestrone diacetate, mestranol, pinestrol, piperazine estrone sulfate, promestriene, quinestrol, tamoxifen, toremifene, raloxifene, lasofoxifene and mixtures thereof.

7. The composition according to claims 1, 2, or 3, characterised in that the gonadotropin releasing hormone composition is triptorelin or a salt thereof and the estrogenic composition is estradiol.

8. The composition of claim 7, characterised in that triptorelin, or a triptorelin salt, is released at a rate of about 100 µg per day and estradiol is released at a rate between about 25 and 50 µg per day.

9. A method for the treatment of prostate cancer comprising:
Administering to a patient suffering from prostate cancer a sustained release formulation of a gonadotropin hormone releasing hormone composition capable of releasing the gonadotropin hormone releasing hormone composition for a period of at least about one month at a rate sufficient to induce and maintain chemical castration of the patient, and

Simultaneously administering to the patient a sustained release formulation of an estrogenic composition capable of maintaining for said period a serum level sufficient to reduce the enhanced loss of bone mineral density or the hot flashes that are normally caused by the administration of a gonadotropin hormone releasing hormone composition that chemically castrates a male patient.

10. A method for the treatment of prostate cancer comprising:

Administering to a patient suffering from prostate cancer a sustained release formulation of a gonadotropin hormone releasing hormone composition capable of releasing the gonadotropin hormone releasing hormone composition for a period of at least about one month at an average rate between about 10 and 1,000 µg per day, and

Simultaneously administering to the patient a sustained release formulation of an estrogenic composition under a profile comprising at least a first initial phase and a second phase, the release of the estrogenic composition in the course of said second phase being at a rate between about 10 and 100 µg of estradiol equivalent per day, the release of the estrogenic composition in the course of said first initial phase never exceeding 5 times the upper daily release of the estrogenic composition occurring during said second phase.

11. A method for the treatment of prostate cancer comprising:

Administering to a patient suffering from prostate cancer a sustained release formulation of a gonadotropin hormone releasing hormone composition capable of releasing the gonadotropin hormone releasing hormone composition for a period of at least about one month at an average rate between about 10 and 1,000 µg per day, and

Simultaneously administering to the patient a sustained release formulation of an estrogenic composition under a profile comprising at least a first initial phase and a second phase, the release of the estrogenic composition in the course of said second phase being at a rate between about 10 and 100 µg of estradiol equivalent per day, the release of the estrogenic composition in the course of said first initial phase never exceeding 5 times the upper daily release of the estrogenic composition occurring during said second phase.

12. A method as in claims 9, 10 or 11, wherein the gonadotropin hormone releasing hormone composition is selected from the group consisting of gonadotropin hormone releasing hormone, agonists of gonadotropin hormone releasing hormone, antagonists of gonadotropin hormone releasing hormone and mixtures thereof.

13. A method as in claims 9, 10 or 11, wherein the gonadotropin hormone releasing hormone composition is a gonadotropin hormone releasing hormone agonist selected from the group consisting leuprorelin, goserelin, triptorelin, buserelin, nafarelin, deslorelin, histerelin, gonadorelin, and salts and mixtures thereof.

14. A method as in claims 9, 10 or 11, wherein the estrogenic composition is selected from the group consisting of chlorotrianisene, dienestrol, diethylstilbestrol, diethylstilbestrol dipropionate, diethylstilbestrol monobenzyl ether, equilelinin, equilelinin sulfate, estetrol, estradiol, (3α,17β)-estr-4-ene-3,17-diol, estriol, estriol hemisuccinate, estrone, estrone sulfate monosodique, estrone potassium sulfate, ethinylestradiol, fosfestrol tetrasodique, hexestrol,

hydroxyestrone diacetate, mestranol, pinestrol, piperazine estrone sulfate, promestriene, quinestrol, tamoxifen, toremifene, raloxifene, lasofoxifene and mixtures thereof.

15. A method as in claims 9, 10 or 11, wherein the gonadotropin releasing hormone composition is triptorelin or a salt thereof and the estrogenic composition is estradiol.

16. A method according to claim 15, wherein triptorelin, or a triptorelin salt, is released at a rate of about 100 µg per day and estradiol is released at a rate between about 25 and 50 µg per day.

17. A method as in claims 9, 10 or 11, wherein the composition is administered by a subcutaneous, intramuscular, or transdermal route.

18. Use of a composition comprising:

a first sustained release formulation of a gonadotropin hormone releasing hormone composition capable of releasing the gonadotropin hormone releasing hormone composition during a period of at least about one month at a rate sufficient to induce and maintain chemical castration of a male patient, and

a second sustained release formulation of an estrogenic composition capable of maintaining for said period a serum level sufficient to reduce the enhanced loss of bone mineral density or the hot flashes that are normally caused by the administration of a gonadotropin hormone releasing hormone composition that chemically castrates a male patient, said serum level in estradiol equivalent being less than about 50 pg/ml.

19. Use of a composition comprising:

a first sustained release formulation of a gonadotropin hormone releasing hormone composition capable of releasing the gonadotropin hormone releasing

hormone composition for a period of at least about one month at an average rate between about 10 and 1,000 µg per day, and

a second sustained release formulation of an estrogenic composition capable of releasing the estrogenic composition under a profile comprising at least a first initial phase and a second phase, the release of the estrogenic composition in the course of said second phase being at a rate between about 10 and 100 µg of estradiol equivalent per day, the release of the estrogenic composition in the course of said first initial phase never exceeding 5 times the upper daily release of the estrogenic composition occurring during said second phase,

for the preparation of a medicament for treatment of prostate cancer in a patient suffering from prostate cancer, said first sustained release formulation and said second sustained release formulation being simultaneously administrated to said patient.

20. The use according to any of the claims 18 or 19, characterised in that the gonadotropin hormone releasing hormone composition is selected from the group consisting of gonadotropin hormone releasing hormone, agonists of gonadotropin hormone releasing hormone, antagonists of gonadotropin hormone releasing hormone and mixtures thereof.

21. The use according to any of the claims 18 or 19, characterised in that the gonadotropin hormone releasing hormone composition is a gonadotropin hormone releasing hormone agonist selected from the group consisting leuprorelin, goserelin, triptorelin, buserelin, nafarelin, deslorelin, histerelin, gonadorelin, and salts and mixtures thereof.

22. The use according to any of the claims 18 or 19, characterised in that the estrogenic composition is selected from the group consisting of chlorotrianisene, dienestrol, diethylstilbestrol, diethylstilbestrol dipropionate, diethylstilbestrol monobenzyl ether, equilelinin, equilelinin sulfate, estetrol, estradiol, (3α,17β)-estr-4-ene-3,17-diol, estriol, estriol hemisuccinate, estrone, estrone sulfate monosodique, estrone potassium sulfate, ethinylestradiol,

fosfestrol tetrasodique, hexestrol, hydroxyestrone diacetate, mestranol, pinestrol, piperazine estrone sulfate, promestriene, quinestrol, tamoxifen, toremifene, raloxifene, lasofoxifene and mixtures thereof.

23. The use according to any of the claims 18 or 19, wherein the gonadotropin releasing hormone composition is triptorelin or a salt thereof and the estrogenic composition is estradiol.

24. The use according to claim 23, wherein triptorelin, or a triptorelin salt, is released at a rate of about 100 µg per day and estradiol is released at a rate between about 25 and 50 µg per day.

25. The use according to any of the claims 18 or 19, wherein the composition is administered by a subcutaneous, intramuscular, or transdermal route.